* * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

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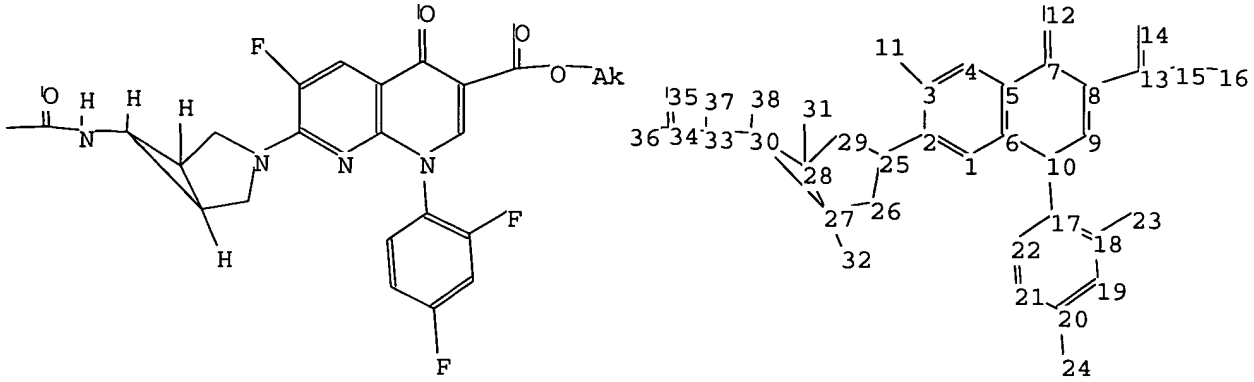
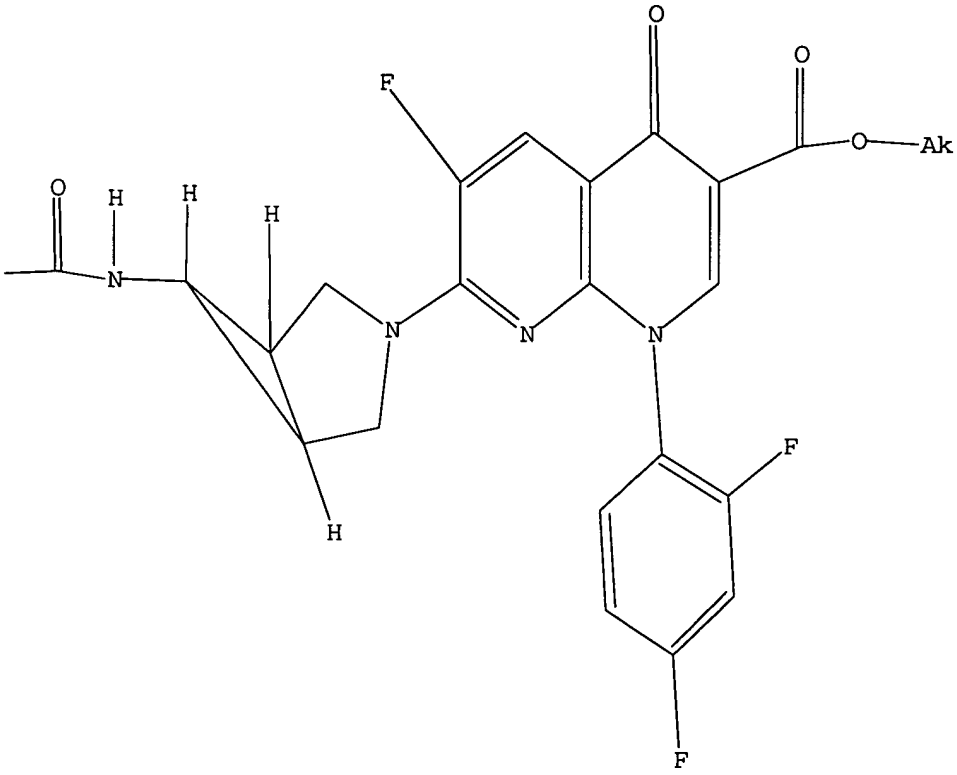


chain nodes :
11 12 13 14 15 16 23 24 31 32 33 34 35 36 37 38
ring nodes :
1 2 3 4 5 6 7 8 9 10 17 18 19 20 21 22 25 26 27 28 29 30
chain bonds :
2-25 3-11 7-12 8-13 10-17 13-14 13-15 15-16 18-23 20-24 27-32 28-31
30-33 30-38 33-34 33-37 34-35 34-36
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 17-18 17-22 18-19 19-20
20-21 21-22 25-26 25-29 26-27 27-28 27-30 28-29 28-30
exact/norm bonds :
2-25 5-7 6-10 7-8 7-12 8-9 9-10 10-17 13-14 13-15 15-16 25-26 25-29
26-27 27-28 27-30 28-29 28-30 30-33 33-34 34-35
exact bonds :
3-11 8-13 18-23 20-24 27-32 28-31 30-38 33-37 34-36
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 17-18 17-22 18-19 19-20 20-21 21-22

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom
19:Atom 20:Atom 21:Atom 22:Atom 23:CLASS 24:CLASS 25:Atom 26:Atom 27:Atom
28:Atom 29:Atom 30:Atom 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS
36:CLASS 37:CLASS 38:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
L4 3 SEA SSS FUL L1

=> file ca

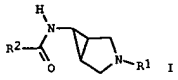
=> s l4
L5 3 L4

=> d ibib abs fhitstr hitrn 1-3

L5 ANSWER 1 OF 3 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:147591 CA
TITLE: Preparation of trovafloxacin
INVENTOR(S): Chiu, Charles K.; Wint, Lewin T.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

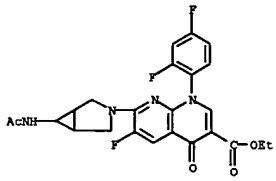
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 6184380	B1	20010206	US 1999-236737		19990125
US 2002095043	A1	20020718	US 2002-87756		20020304
PRIORITY APPLN. INFO.:			US 1998-71601P	P	19980116
			US 1999-236737	A3	19990125
			US 2000-718324	A3	20001122

OTHER SOURCE(S): CASREACT 134:147591; MARPAT 134:147591
GI



AB The title process comprises use of azabicyclohexanes I [R1 = (un)substituted CH2Ph; R2 = CF3, alkyl, (un)substituted Ph] and a 7-chloro-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid alkyl ester.
IT **323575-31-1P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of trovafloxacin)
RN 323575-31-1 CA
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[6-(acetylamino)-3-azabicyclo[3.1.0]hex-3-yl]-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)

L5 ANSWER 1 OF 3 CA COPYRIGHT 2005 ACS on STN (Continued)

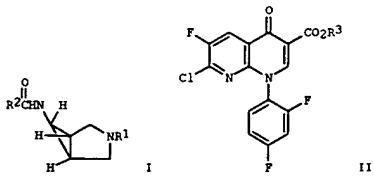


IT **323575-31-1P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of trovafloxacin)
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 3 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:116223 CA
TITLE: Process for preparing naphthyridones and intermediates
INVENTOR(S): Chiu, Charles Kwok-Fung; Wint, Lewin Theophilus
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 930297	A1	19990721	EP 1999-300183		19990112
EP 930297	B1	20030423			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
AU 9897115	A1	19990805	AU 1998-97115		19981215
JP 11255745	A2	19990921	JP 1999-5494		19990112
SG 76584	A1	20001121	SG 1999-46		19990112
EG 21514	A	20011128	EG 1999-34		19990112
TW 483890	B	20020421	TW 1999-88100415		19990112
AT 238281	E	20030515	AT 1999-300183		19990112
PT 930297	T	20030829	PT 1999-300183		19990112
ES 2195513	T3	20031201	ES 1999-300183		19990112
BR 9900066	A	20000509	BR 1999-66		19990114
CA 2258960	C	20020903	CA 1999-2258960		19990114
CA 2258960	AA	19990716			
NO 9900185	A	19990719	NO 1999-185		19990115
CN 1228422	A	19990915	CN 1999-101086		19990115
NZ 333769	A	20000327	NZ 1999-333769		19990115
ZA 9900277	A	20000717	ZA 1999-277		19990115
BG 64094	B1	20031231	BG 1999-103087		19990115
PRIORITY APPLN. INFO.:			US 1998-71601P	P	19980116

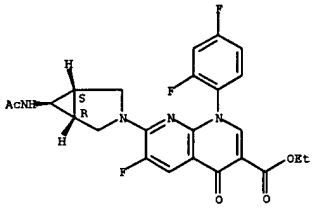
OTHER SOURCE(S): CASREACT 131:116223; MARPAT 131:116223
GI



AB 6-Acetamido-3-benzylazabicyclo[3.1.0]hexanes [I; R1 = (un)substituted PhCH2; R2 = C1-6 alkyl, CF3, (un)substituted Ph] are prepared by reduction of
the parent nitro derivs. with Fe powder in AcOH/Me2CHOH and N-acylation of the resulting amines. Debenzylation of I with H in AcOH in the presence of Pd catalyst, condensation of debenzylated intermediates with naphthyridine-3-carboxylate esters (II; R3 = C1-6 alkyl) and hydrolysis of

L5 ANSWER 2 OF 3 CA COPYRIGHT 2005 ACS on STN (Continued)
the resulting intermediates (prepn. procedure claimed) with MeSO3H in aq. org. solvents gives trovafloxacin (III), an antibacterial active esp. against gram-pos. bacterial strains, as monomethanesulfonate salt. Thus, III·HO3SMe was prepd. from I (R1 = PhCH2, R2 = Me) and II (R3 = Et) as described above.
IT **232598-25-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis with methanesulfonic acid; process for preparing
naphthyridones and trovafloxacin intermediates)
RN 232598-25-3 CA
CN 1,8-Naphthyridine-3-carboxylic acid, 7-[(1α,5α,6α)-6-(acetylamino)-3-azabicyclo[3.1.0]hex-3-yl]-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **232598-25-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis with methanesulfonic acid; process for preparing
naphthyridones and trovafloxacin intermediates)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 3 CA COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 126:157823 CA
TITLE: Process for preparing azabicyclo naphthyridine carboxylic acid dipeptide prodrug
INVENTOR(S): Braish, Tamim F.; Castaldi, Michael J.; Watson, Harry A., Jr.
PATENT ASSIGNEE(S): Pfizer Inc., USA; Braish, Tamim F.; Castaldi, Michael J.; Watson, Harry A., Jr.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9700268	A1	19970103	WO 1996-IB257	19960327
W: CA, JP, MX, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2224616	AA	19970103	CA 1996-2224616	19960327
CA 2224616	C	20000502		
EP 833837	A1	19980408	EP 1996-904996	19960327
EP 833837	B1	20020731		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 3029293	B2	20000404	JP 1997-502832	19960327
JP 10511983	T2	19981117		
AT 221544	E	20020815	AT 1996-904996	19960327
PT 833837	T	20021129	PT 1996-904996	19960327
ES 2178701	T3	20030101	ES 1996-904996	19960327
US 5939550	A	19990817	US 1998-981350	19980311
PRIORITY APPLN. INFO.:			US 1995-490827 A1	19950615
			WO 1996-IB257 W	19960327

OTHER SOURCE(S): MARPAT 126:157823
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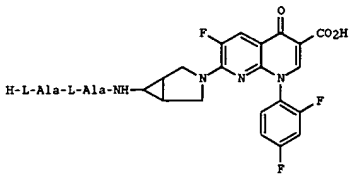


I

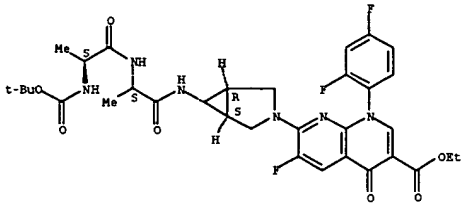
AB A process is given for preparing a pharmaceutically acceptable acid addition salt of prodrug acid I. Thus, N-Boc protected 7-[(1α, 5α, 6α)-6-amino-3-azabicyclo[3.1.0]hex-3-yl]-6-fluoro-1-(2,4-difluorophenyl)-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid Et ester, Boc-Q-OEt, (Boc = tert-butoxycarbonyl) was deprotected by

L5 ANSWER 3 OF 3 CA COPYRIGHT 2005 ACS on STN (Continued)
trifluoroacetic acid and the product coupled with Boc-Ala-Ala-OH using EEDQ and then treated with methanesulfonic acid to afford I mesylate. The latter prodrug serves as a water-sol. prodrug companion to known antibacterial agent H-Q-OH.

IT **186772-86-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn.of azabicyclo naphthyridine carboxylic acid dipeptide prodrug)

RN 186772-86-1 CA
CN L-Alaninamide, N-[(1,1-dimethylethoxy)carbonyl]-L-alanyl-N-[(1α,5α,6α)-3-[8-(2,4-difluorophenyl)-6-(ethoxycarbonyl)-3-fluoro-5,8-dihydro-5-oxo-1,8-naphthyridin-2-yl]-3-azabicyclo[3.1.0]hex-6-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **186772-86-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn.of azabicyclo naphthyridine carboxylic acid dipeptide prodrug)

10/087,756

```
=> file casreact

=> s l1 full
FULL SEARCH INITIATED 11:10:33 FILE 'CASREACT'
SCREENING COMPLETE -    121 REACTIONS TO VERIFY FROM      6 DOCUMENTS

100.0% DONE    121 VERIFIED      10 HIT RXNS                    2 DOCS
SEARCH TIME: 00.00.01

L7            2 SEA SSS FUL L1 (    10 REACTIONS)

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L7 ANSWER 1 OF 2 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:147591 CASREACT
TITLE: Preparation of trovafloxacin
INVENTOR(S): Chiu, Charles K.; Wint, Lewin T.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6184380	B1	20010206	US 1999-236737	19990125
US 2002095043	A1	20020718	US 2002-87756	20020304
PRIORITY APPLN. INFO.:			US 1998-71601P	19980116
			US 1999-236737	19990125
			US 2000-718324	20001122

OTHER SOURCE(S): MARPAT 134:147591
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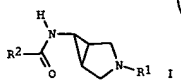


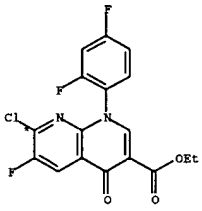
I

AB The title process comprises use of azabicyclohexanes I [R1 = (un)substituted CH2Ph; R2 = CF3, alkyl, (un)substituted Ph] and a 7-chloro-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid alkyl ester.

RX(3) OF 14 ...J + M ===> M...

J: CM 1

J: CM 2



M

L7 ANSWER 1 OF 2 CASREACT COPYRIGHT 2005 ACS on STN (Continued)

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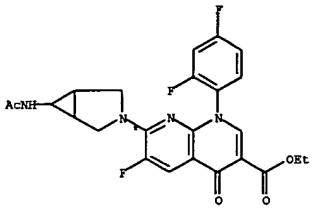


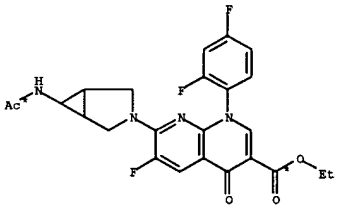
N
YIELD 95%

RX(3) RCT J 323575-30-0, M 100491-29-0

STAGE(1)
RGT O 121-44-8 Et3N
SOL 141-78-6 AcOEt

STAGE(2)
SOL 7732-18-5 Water
PRO N **323575-31-1**

RX(4) OF 14 ...M ===> Q



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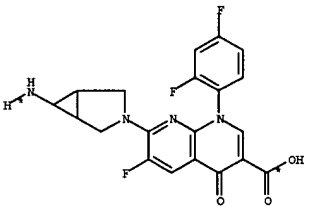
(4) →

L7 ANSWER 1 OF 2 CASREACT COPYRIGHT 2005 ACS on STN (Continued)

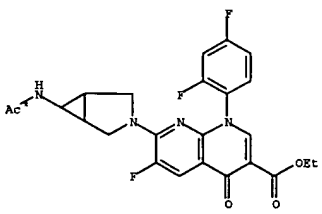
Q: CM 1



Q: CM 2

RX(4) RCT N **323575-31-1**
RGT R 75-75-2 MeSO3H
PRO Q 323575-32-2
SOL 71-36-3 BuOH, 7732-18-5 Water

RX(5) OF 14 ...M ===> T

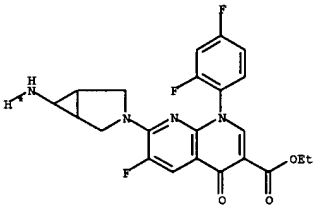


N

(5) →

T: CM 1
YIELD 96%

L7 ANSWER 1 OF 2 CASREACT COPYRIGHT 2005 ACS on STN (Continued)



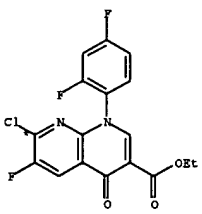
T: CM 2
YIELD 96%

RX(5) RCT N **323575-31-1**
RGT R 75-75-2 MeSO3H
PRO T 323575-34-4
SOL 64-17-5 EtOH

RX(7) OF 14 COMPOSED OF RX(2), RX(3)
RX(7) C + E + M ===> M

C

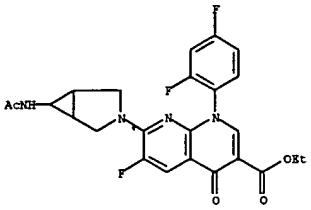
E



M

2
STEPS →

L7 ANSWER 1 OF 2 CASREACT COPYRIGHT 2005 ACS on STN (Continued)



N
YIELD 95%

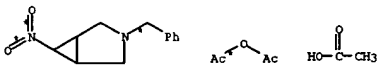
RX(2) RCT C 323575-28-6, E 64-19-7
RGT K 1333-74-0 H2
PRO J 323575-30-0
CAT 7440-05-3 Pd
SOL 7732-18-5 Water

RX(3) RCT J 323575-30-0, M 100491-29-0

STAGE(1)
RGT O 121-44-8 Et3N
SOL 141-78-6 AcOEt

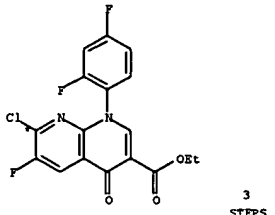
STAGE(2)
SOL 7732-18-5 Water
PRO N 323575-31-1

RX(10) OF 14 COMPOSED OF RX(1), RX(2), RX(3)
RX(10) A + B + E + M ===> N



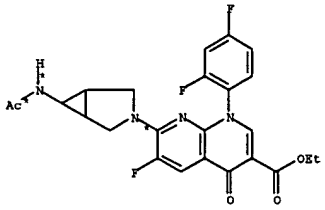
A B E

L7 ANSWER 1 OF 2 CASREACT COPYRIGHT 2005 ACS on STN (Continued)



M

3 STEPS



N
YIELD 95%

RX(1) RCT A 323575-35-5

STAGE(1)
RGT D 7439-89-6 Fe, E 64-19-7 AcOH
SOL 67-63-0 Me2CHOH

STAGE(2)
RCT B 108-24-7

STAGE(3)
RGT F 1310-73-2 NaOH
SOL 7732-18-5 Water, 75-09-2 CH2Cl2
PRO C 323575-28-6

RX(2) RCT C 323575-28-6, E 64-19-7

L7 ANSWER 1 OF 2 CASREACT COPYRIGHT 2005 ACS on STN (Continued)

RGT K 1333-74-0 H2
PRO J 323575-30-0
CAT 7440-05-3 Pd
SOL 7732-18-5 Water

RX(3) RCT J 323575-30-0, M 100491-29-0

STAGE(1)
RGT O 121-44-8 Et3N
SOL 141-78-6 AcOEt

STAGE(2)
SOL 7732-18-5 Water
PRO N 323575-31-1

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/087,756

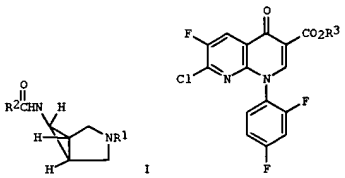
=> d ibib abs rx 2

L7 ANSWER 2 OF 2 CASREACT COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 131:116223 CASREACT
TITLE: Process for preparing naphthyridones and intermediates
INVENTOR(S): Chiu, Charles Kwok-Fung; Wint, Lewin Theophilus
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 930297	A1	19990721	EP 1999-300183	19990112
EP 930297	B1	20030423		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 9897115	A1	19990805	AU 1998-97115	19981215
JP 11255745	A2	19990921	JP 1999-5494	19990112
SG 76584	A1	20001121	SG 1999-46	19990112
EG 21514	A	20011128	EG 1999-34	19990112
TW 483890	B	20020421	TW 1999-88100415	19990112
AT 238281	E	20030515	AT 1999-300183	19990112
PT 930297	T	20030829	PT 1999-300183	19990112
ES 2195513	T3	20031201	ES 1999-300183	19990112
BR 9900066	A	20000509	BR 1999-66	19990114
CA 2258960	C	20020903	CA 1999-2258960	19990114
CA 2258960	AA	19990716		
NO 9900185	A	19990719	NO 1999-185	19990115
CN 1228422	A	19990915	CN 1999-101086	19990115
NZ 333769	A	20000327	NZ 1999-333769	19990115
ZA 9900277	A	20000717	ZA 1999-277	19990115
BG 64094	B1	20031231	BG 1999-103087	19990115

PRIORITY APPLN. INFO.: US 1998-71601P 19980116
OTHER SOURCE(S): MARPAT 131:116223
GI



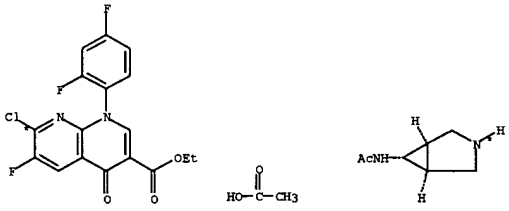
I II

AB 6-Acetamido-3-benzylazabicyclo[3.1.0]hexanes [I; R1 = (un)substituted

L7 ANSWER 2 OF 2 CASREACT COPYRIGHT 2005 ACS on STN (Continued)

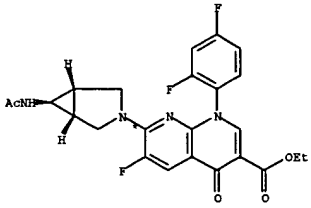
PRO H 232598-23-1
SOL 64-17-5 EtOH

RX(4) OF 14 ...R + B ===> G...



R B: CM 1 B: CM 2

(4)



G
YIELD 95%

RX(4) RCT R 100491-29-0, B 232613-59-1

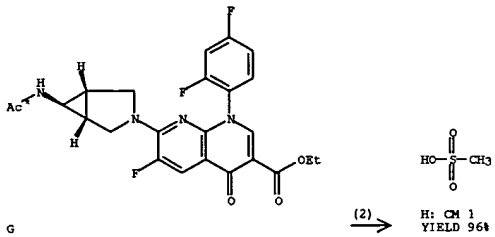
STAGE(1)
RGT S 121-44-8 Et3N
SOL 141-78-6 AcOEt

STAGE(2)
RGT P 7732-18-5 Water
PRO G 232598-25-3

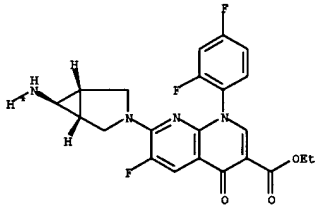
L7 ANSWER 2 OF 2 CASREACT COPYRIGHT 2005 ACS on STN (Continued)

PhCH2; R2 = C1-6 alkyl, CF3, (un)substituted Ph] are prepd. by redn. of the parent nitro derivs. with Fe powder in AcOH/Me2CHOH and N-acylation of the resulting amines. Debenzylation of I with H in AcOH in the presence of Pd catalyst, condensation of debenzylated intermediates with naphthyridine-3-carboxylate esters (II; R3 = C1-6 alkyl) and hydrolysis of the resulting intermediates (prepn. procedure claimed) with MeSO3H in aq. org. solvents gives trovafloxacin (III), an antibacterial active esp. against gram-pos. bacterial strains, as monomethanesulfonate salt. Thus, III·HO3SMe was prepd. from I (R1 = PhCH2, R2 = Me) and II (R3 = Et) as described above.

RX(2) OF 14 ...G ===> H



G H: CM 1
YIELD 96%

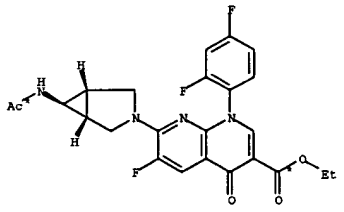


H: CM 2
YIELD 96%

RX(2) RCT G 232598-25-3
RGT I 75-75-2 MeSO3H

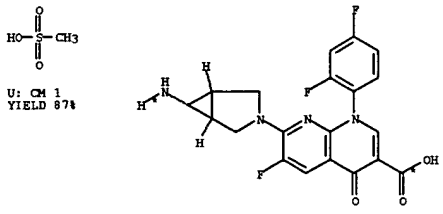
L7 ANSWER 2 OF 2 CASREACT COPYRIGHT 2005 ACS on STN (Continued)

RX(5) OF 14 ...G ===> U



G

(5)



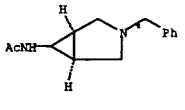
U: CM 1
YIELD 87%

U: CM 2
YIELD 87%

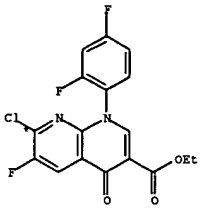
RX(5) RCT G 232598-25-3
RGT I 75-75-2 MeSO3H
PRO U 147059-75-4
SOL 7732-18-5 Water, 71-36-3 BuOH
NTE extensive work-up to change crystal properties

RX(6) OF 14 COMPOSED OF RX(1), RX(4)
RX(6) A + R ===> G

L7 ANSWER 2 OF 2 CASREACT COPYRIGHT 2005 ACS on STN (Continued)

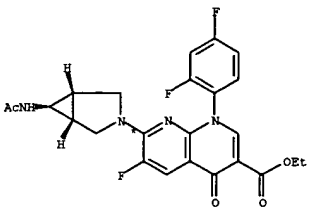


A



R

2 STEPS



G
YIELD 95%

RX(1) RCT A 232598-24-2

STAGE(1)
RGT C 64-19-7 AcOH
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH

STAGE(2)
RGT D 1333-74-0 H2
PRO B 232613-59-1

RX(4) RCT R 100491-29-0, B 232613-59-1

STAGE(1)
RGT S 121-44-8 Et3N

L7 ANSWER 2 OF 2 CASREACT COPYRIGHT 2005 ACS on STN (Continued)

RX(3) RCT K 13021-02-8

STAGE(1)
RGT M 7439-89-6 Fe, C 64-19-7 AcOH
SOL 67-63-0 Me2CHOH

STAGE(2)
RCT L 108-24-7

STAGE(3)
SOL 67-63-0 Me2CHOH

STAGE(4)
RGT N 1310-73-2 NaOH
SOL 7732-18-5 Water, 107-06-2 ClCH2CH2Cl
PRO A 232598-24-2

RX(1) RCT A 232598-24-2

STAGE(1)
RGT C 64-19-7 AcOH
CAT 7440-05-3 Pd
SOL 67-56-1 MeOH

STAGE(2)
RGT D 1333-74-0 H2
PRO B 232613-59-1

RX(4) RCT R 100491-29-0, B 232613-59-1

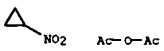
STAGE(1)
RGT S 121-44-8 Et3N
SOL 141-78-6 AcOEt

STAGE(2)
RGT P 7732-18-5 Water
PRO G 232598-25-3

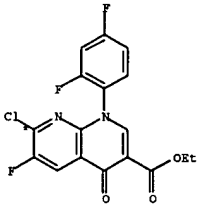
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 CASREACT COPYRIGHT 2005 ACS on STN (Continued)

RX(14) OF 14 COMPOSED OF RX(3), RX(1), RX(4)
RX(14) K + L + R ===> G

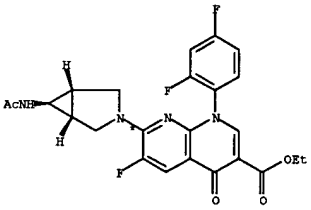


K L



R

3 STEPS



G
YIELD 95%

10/087,756

=>
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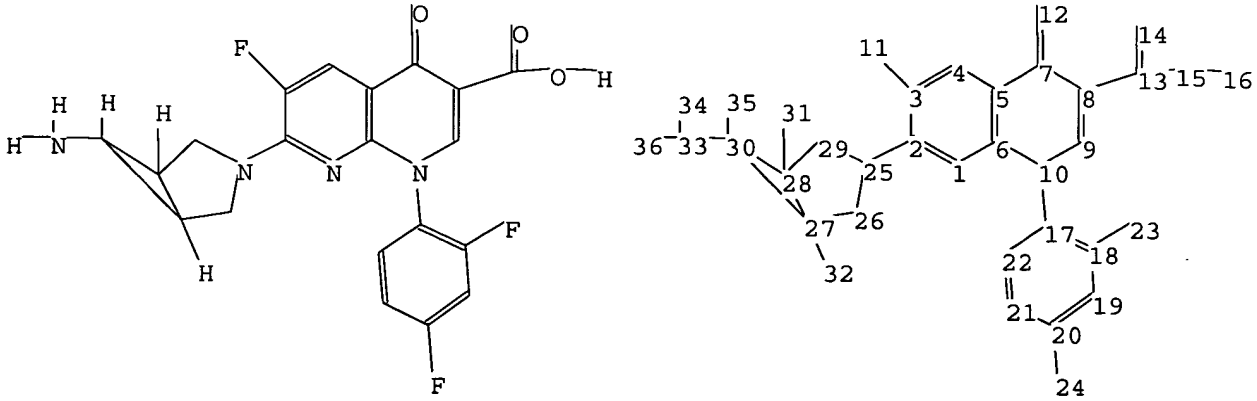
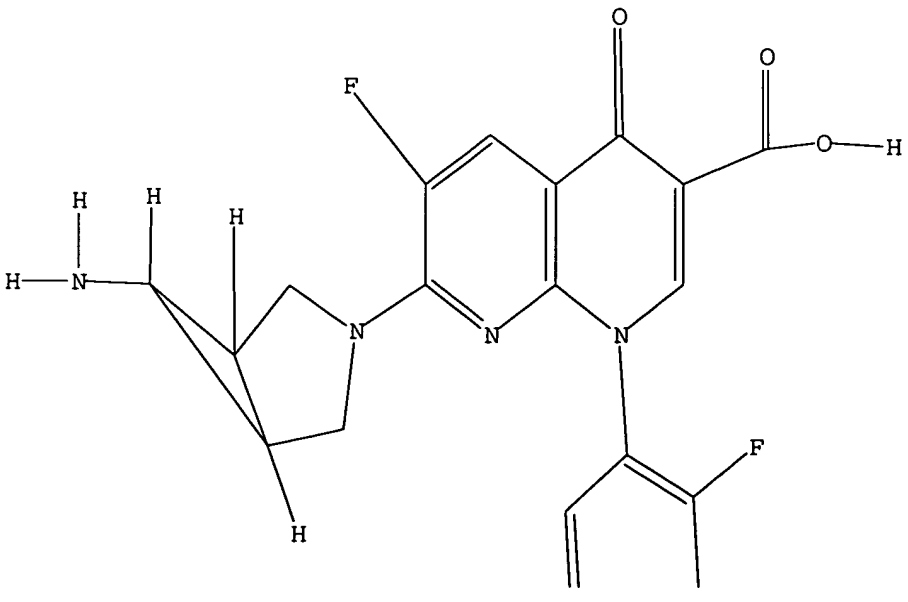


L8 STRUCTURE UPLOADED

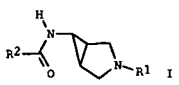
=> d l8
L8 HAS NO ANSWERS
L8 STR



L9 ANSWER 1 OF 5 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 134:147591 CASREACT
TITLE: Preparation of trovafloxacin
INVENTOR(S): Chiu, Charles K.; Wint, Lewin T.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6184380	B1	20010206	US 1999-236737	19990125
US 2002095043	A1	20020718	US 2002-87756	20020304
PRIORITY APPLN. INFO.:			US 1998-71601P	19980116
			US 1999-236737	19990125
			US 2000-718324	20001122

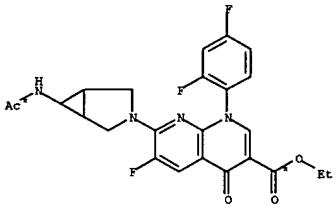
OTHER SOURCE(S): MARPAT 134:147591
GI



I

AB The title process comprises use of azabicyclohexanes I [R1 = (un)substituted CH2Ph; R2 = CF3, alkyl, (un)substituted Ph] and a 7-chloro-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid alkyl ester.

RX(4) OF 14 ...N ===> Q

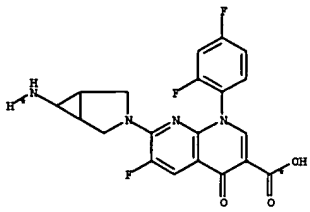


N

(4)

L9 ANSWER 1 OF 5 CASREACT COPYRIGHT 2005 ACS on STN (Continued)

Q: CM 1



Q: CM 2

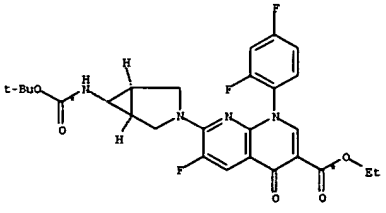
RX(4) RCT N 323575-31-1
RGT R 75-75-2 MeSO3H
PRO Q 323575-32-2
SOL 71-36-3 BuOH, 7732-18-5 Water
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 5 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 133:222629 CASREACT
TITLE: Synthesis of trovafloxacin using various (1α,5α,6α)-3-azabicyclo[3.1.0]hexane derivatives
AUTHOR(S): Norris, Timothy; Braish, Tamim F.; Butters, Michael; DeVries, Keith M.; Hawkins, Joel M.; Massett, Stephen S.; Rose, Peter R.; Santafianos, Dinos; Sklavounos, Constantine
CORPORATE SOURCE: Pfizer Central Research Laboratories, Groton, CT, 06340, USA
SOURCE: Perkin 1 (2000), (10), 1615-1622
CODEN: PERKF9
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Trovafloxacin, a novel broad spectrum antibacterial, contains the unusual (1α,5α,6α)-3-azabicyclo[3.1.0]hexane ring system. The prototype of the industrial synthesis of this ring system and possible mechanistic pathways to exclusive formation of the exo or 6α-nitro derivative I are described, which leads to the key 6α-nitro-3-azabicyclo[3.1.0]hexane intermediate [II; R1 = NO2, R2 = Bn (III)]. The synthesis of II (R1 = NH2, R2 = H) and useful protected exo 6-amino derivs. II (R1 = BOCNH, PHCH:N; R2 = H) follows from III. These can be coupled with the 7-chloronaphthyridone to yield protected trovafloxacin compds. IV [R3 = BOCNH, NH2, PHCH:N] in good yield. Removal of protecting groups from IV with methanesulfonic acid yields trovafloxacin mesylate from which the trovafloxacin zwitterion can be liberated with base treatment. The zwitterion can also be prepared directly from the tosylate salt of II (R1 = NH2, R2 = H) and naphthyridone-2-carboxylic acid V.

RX(16) OF 68 ...AM ===> AS...

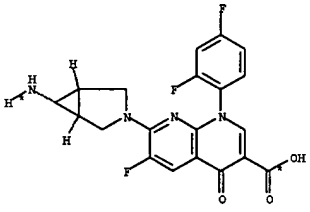


AM

(16)

L9 ANSWER 2 OF 5 CASREACT COPYRIGHT 2005 ACS on STN (Continued)

AS: CM 1
YIELD 90%



AS: CM 2
YIELD 90%

RX(16) RCT AM 134575-66-9
RGT AT 75-75-2 MeSO3H
PRO AS 147059-75-4
SOL 109-99-9 THF
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 5 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 132:122609 CASREACT
TITLE: Preparation of trovafloxacin and analogs
INVENTOR(S): Norris, Timothy
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 976749	A1	20000202	EP 1999-305577	19990714
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6114531	A	20000905	US 1999-324385	19990602
JP 2000053646	A2	20000222	JP 1999-210179	19990726
CA 2278845	C	20030708	CA 1999-2278845	19990726
CA 2278845	AA	20000128		
AU 9941169	A1	20000217	AU 1999-41169	19990727
KR 2000012002	A	20000225	KR 1999-30560	19990727
BR 9903003	A	20000321	BR 1999-3003	19990727
CN 1247865	A	20000322	CN 1999-119527	19990727
ZA 9904814	A	20010129	ZA 1999-4814	19990727
RU 2167867	C2	20010527	RU 1999-116268	19990727
TR 9901796	A2	20000221	TR 1999-9901796	19990728
MX 9907034	A	20000228	MX 1999-7034	19990728

PRIORITY APPLN. INFO.: US 1998-94440P 19980728
OTHER SOURCE(S): MARPAT 132:122609
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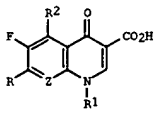
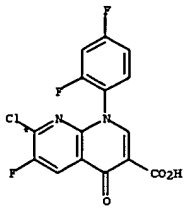


I

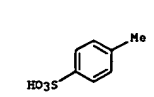
AB Title compds. [I; R = H2N(CH2)nZ1; R1 = Et, CMe3, cyclopropyl, etc.; R2 = H, F, alkyl, alkoxy, etc.; Z = CH, CF, CR3, N, etc.; R1R3 = atoms to complete a ring; Z1 = 1-aza(bi)cycloalkylene; n = 0 or 1] were prepared by condensation of I (R = halo) with an acid salt of H2N(CH2)nZ1H.

RX(6) OF 36 ...U + S ===> V

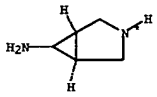
L9 ANSWER 3 OF 5 CASREACT COPYRIGHT 2005 ACS on STN (Continued)



U

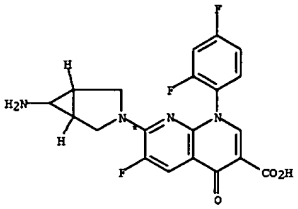


S: CM 1



S: CM 2

(6)



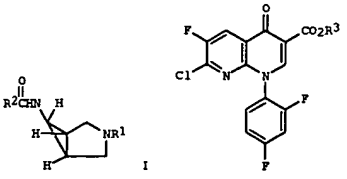
V
YIELD 75%

RX(6) RCT U 100492-04-4, S 256369-34-3
STAGE(1)
RGT W 121-44-8 Et3N
SOL 67-56-1 MeOH
STAGE(2)
SOL 109-99-9 THF
PRO V 147059-72-1
NTE STEREOSELECTIVE
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 5 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 131:116223 CASREACT
TITLE: Process for preparing naphthyridones and intermediates
INVENTOR(S): Chiu, Charles Kwok-Fung; Wint, Lewin Theophilus
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 930297	A1	19990721	EP 1999-300183	19990112
EP 930297	B1	20030423		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 9897115	A1	19990805	AU 1998-97115	19981215
JP 11255745	A2	19990921	JP 1999-5494	19990112
SG 76584	A1	20001121	SG 1999-46	19990112
EG 21514	A	20011128	EG 1999-34	19990112
TW 483890	B	20020421	TW 1999-88100415	19990112
AT 238281	E	20030515	AT 1999-300183	19990112
PT 930297	T	20030829	PT 1999-300183	19990112
ES 2195513	T3	20031201	ES 1999-300183	19990112
BR 9900066	A	20000509	BR 1999-66	19990114
CA 2258960	C	20020903	CA 1999-2258960	19990114
CA 2258960	AA	19990716		
NO 9900185	A	19990719	NO 1999-185	19990115
CN 1228422	A	19990915	CN 1999-101086	19990115
NZ 333769	A	20000327	NZ 1999-333769	19990115
ZA 9900277	A	20000717	ZA 1999-277	19990115
BG 64094	B1	20031231	BG 1999-103087	19990115

PRIORITY APPLN. INFO.: US 1998-71601P 19980116
OTHER SOURCE(S): MARPAT 131:116223
GI

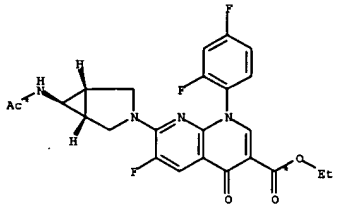


I II

AB 6-Acetamido-3-benzylazabicyclo[3.1.0]hexanes [I; R1 = (un)substituted PhCH2; R2 = C1-6 alkyl, CF3, (un)substituted Ph] are prepared by reduction of the parent nitro derivs. with Fe powder in AcOH/Me2CHOH and N-acylation of the resulting amines. Debenzylation of I with H in AcOH in the presence of Pd catalyst, condensation of debenzylated intermediates with naphthyridine-3-carboxylate esters (II; R3 = C1-6 alkyl) and hydrolysis of

L9 ANSWER 4 OF 5 CASREACT COPYRIGHT 2005 ACS on STN (Continued)
the resulting intermediates (prepn. procedure claimed) with MeSO3H in aq. org. solvents gives trovafloxacin (III), an antibacterial active esp. against gram-pos. bacterial strains, as monomethanesulfonate salt. Thus, III·HO3SMe was prepd. from I (R1 = PhCH2, R2 = Me) and II (R3 = Et) as described above.

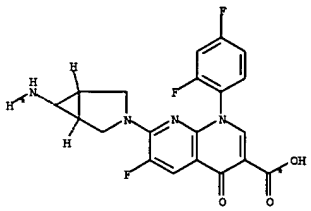
RX(5) OF 14 ...G ===> U



G

(5)

U: CM 1
YIELD 87%

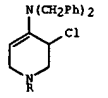


U: CM 2
YIELD 87%

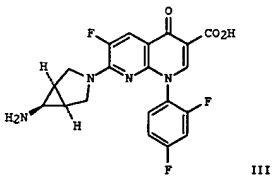
RX(5) RCT G 232598-25-3
RGT I 75-75-2 MeSO3H
PRO U **147059-75-4**
SOL 7732-18-5 Water, 71-36-3 BuOH
NTE extensive work-up to change crystal properties
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 5 CASREACT COPYRIGHT 2005 ACS on STN (Continued)

L9 ANSWER 5 OF 5 CASREACT COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 129:122591 CASREACT
TITLE: Diastereoselective syntheses of N-protected derivatives of 1α,5α,6β-6-amino-3-azabicyclo[3.1.0]hexane. A route to trovafloxacin 6β-diastereomer
AUTHOR(S): Vilsmaier, Elmar; Goerz, Torsten
CORPORATE SOURCE: Fachbereich Chemie, Universitaet Kaiserslautern, Kaiserslautern, D-67663, Germany
SOURCE: Synthesis (1998), (5), 739-744
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



II

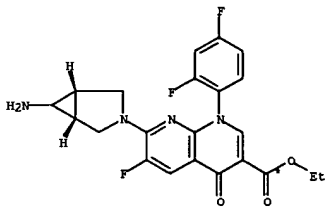


III

AB N-protected derivs. of 1α,5α,6β-6-amino-3-azabicyclo[3.1.0]hexane (I) were synthesized via chloro enamines II (R = PhCH2, allyl). Specific N-protection was realized either by using a chloro enamine with different protecting groups or by selective removal of identical protecting groups at tribenzylated I. N,N'-dibenzylated I allowed the preparation of naphthyridine III.MeSO3H which represents the 6β-diastereomer of trovafloxacin mesylate, a potent Gyrase inhibitor.

RX(14) OF 75 ...AP ===> AS

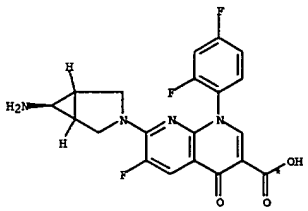
L9 ANSWER 5 OF 5 CASREACT COPYRIGHT 2005 ACS on STN (Continued)



AP

(14)

AS: CM 1
YIELD 60%



AS: CM 2
YIELD 60%

RX(14) RCT AP 210236-57-0
RGT AT 75-75-2 MeSO3H
PRO AS **147126-01-0**
SOL 7732-18-5 Water

10/087,756

```
=> d his

     (FILE 'HOME' ENTERED AT 11:08:38 ON 18 APR 2005)

     FILE 'REGISTRY' ENTERED AT 11:08:42 ON 18 APR 2005
L1             STRUCTURE UPLOADED
L2           0 S L1SAM
L3           0 S L1 SAM
L4           3 S L1 FULL

     FILE 'CA' ENTERED AT 11:09:13 ON 18 APR 2005
L5           3 S L4

     FILE 'CASREACT' ENTERED AT 11:10:22 ON 18 APR 2005
L6           0 S L1
L7           2 S L1 FULL
L8             STRUCTURE UPLOADED
L9           5 S L8 FULL

=>

---Logging off of STN---


=>
Executing the logoff script...
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